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SUMMARY OF SAFETY AND EFFECTIVENESS

GEN-PROBE® APTIMA® Adapter Kit

General Information

Submitted By:	Company Contact:
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Trade Name: GEN-PROBE® APTIMA® Adapter Kit

Common or Usual Name: Transport medium/diluent to allow testing of specimens collected with GEN-PROBE PACE collection devices in the GEN-PROBE APTIMA Combo 2 Assay, an rRNA Target-amplified nucleic acid probe test for the *in vitro* diagnostic detection of *Chlamydia trachomatis* and/or *Neisseria Gonorrhoeae*

Classification Names: DNA reagents, Chlamydia and DNA reagents, Neisseria (Microbiology Classification Device List)

Classification Codes:

Class I

Panel: Microbiology
Number: CFR 866.3120
Name: DNA Reagents, Chlamydia

Reagents used to identify *Chlamydia* directly from clinical specimens and/or cultured isolates derived from clinical specimens.

Class II

Panel: Microbiology
Number: CFR 866.3390
Name: DNA Reagents, Neisseria

Reagents used to identify *N. gonorrhoeae* directly from clinical specimens and/or culture isolates derived from clinical specimens.

Substantially Equivalent Devices: Tissue culture media and components, synthetic cells and tissue culture.

Device Description

The APTIMA Adapter Kit is specifically formulated to allow testing of specimens collected with the GEN-PROBE PACE collection devices in the APTIMA Combo 2 Assay. The APTIMA Adapter Kit provides a diluent for PACE specimens. The diluent is identical to the transport media provided in both the PACE and APTIMA collection kits. The APTIMA Adapter Kit can **only** be used in conjunction with the GEN-PROBE PACE Specimen Collection Kits for testing in the APTIMA Combo 2 Assay. The description provided pertains to the test application (the APTIMA Combo 2 Assay).

Background on the Disease and Principle of the APTIMA Combo 2 Assay

The Disease

Chlamydiae are nonmotile, gram-negative, obligate intracellular bacteria with a unique development cycle that differentiates them from other microorganisms. Chlamydiae rely on adenosine triphosphate (ATP) in host cells for replication. The development cycle involves 2 major forms of the organism: the infective nondividing elementary body that can survive in the extracellular environment, and the noninfective reticulate body that divides intracellularly by binary fission.

C. trachomatis infections are a major cause of sexually transmitted diseases (STD) in the United States. More than 580,000 new cases of chlamydial infections were reported in 1999 [CDC, 1999]. In humans, *C. trachomatis* species are responsible for infections of the cervix, urethra, and upper genital tract in women, infections of the urethra and epididymis in men, and conjunctivitis and pneumonia in newborns [Schachter, J. and M. Grossman, 1981].

N. gonorrhoeae, or gonococci, are gram-negative diplococci with adjacent sides flattened that give a characteristic kidney shape appearance (Knapp and Rice, 1995). The cells are nonmotile and do not produce endospores. The majority of infections are uncomplicated lower genital tract infections. Left untreated in women, infections can ascend and cause Pelvic Inflammatory Disease (PID). PID can manifest as endometritis, salpingitis, pelvic peritonitis, and tubo-ovarian abscesses (Hook, 1985). A smaller percentage of persons

with gonococcal infections may develop Disseminated Gonococcal Infection (Hook, 1985).

Screening for the presence of these diseases is the cornerstone for prevention strategies. A large number of these cases may be asymptomatic or have symptoms that are not specific; this makes reduction of the prevalence of chlamydial and gonococcal infections difficult. An accurate and prompt diagnosis of these infections is important to ensure appropriate patient management, to prevent disease complications and their associated medical costs, and to control transmission to uninfected partners.

Historical and Conventional Methods

The culture method is no longer considered to be the gold standard for diagnosing infection with *C. trachomatis*. Amplification methods have been developed and shown to be more sensitive than culture. The APTIMA Combo 2 Assay utilizes Transcription-Mediated Amplification (TMA) and Hybridization Protection Assay (HPA) to detect ribosomal RNA (rRNA) directly from clinical samples. Other amplification-based assays use a similar approach of directly amplifying a target molecule directly from clinical specimens.

Culture for *C. trachomatis* is considered 100% specific when performed by competent laboratories [Review Criteria for Assessment of In Vitro Diagnostic Devices for Direct Detection of Chlamydiae in Clinical Specimens, original ver. 2.1, January, 1992], but the technical requirements and time-to-result limit the utility of culture for screening programs.

Non-culture diagnostic tests make more aggressive screening and prevention strategies possible because of their ease of use, shorter time-to-result, and absence of viability requirements. Nonculture methods for *C. trachomatis* detection include direct fluorescent antibody staining (DFA), enzyme immunoassay (EIA), nonamplified nucleic acid hybridization (probe assays), PCR, LCR, and SDA.

Conventional diagnosis of *N. gonorrhoeae* infection requires isolation of the organism on selective media or the observation of diplococci in Gram smears [Hook, 1985]. Culture is inexpensive and relatively sensitive. However it can be problematic. Improper specimen storage and transport can result in the loss of viability. Poor sampling technique, toxic sampling equipment, and the inhibition of growth by components of body secretions can result in false negative results [Bassiri, 1997]. Nonculture methods for *N. gonorrhoeae* detection include enzyme immunoassay (EIA), nonamplified nucleic acid hybridization (probe assays), PCR, LCR, and SDA.

Patient Care and Public Health Implications

C. trachomatis and *N. gonorrhoeae* infections are the most common sexually transmitted infections in the world, with an estimated 582,000 new cases of C. trachomatis infections and 323,000 new cases of *N. gonorrhoeae* in the U.S. in 1999 [CDC, 2000]. *C. trachomatis* can cause infections of the cervix, urethra and upper genital tract in women, and can lead to PID, ectopic pregnancy and infertility.

Chlamydia can also cause epididymitis in men, and conjunctivitis and pneumonia in newborns. The prevalence of chlamydial infections ranges from 3 to 5% among asymptomatic men and women to 10 to 20% among adolescents in STD clinics [Van Der Pol, 2000; Crotchfelt, 1998; Quinn, T.C. 1995; Quinn, T.C. and W. Cates, 1992; Schachter, J. and M. Grossman, 1981]. *N. gonorrhoeae* can cause PID and Disseminated Gonococcal Infection (DGI). The incidence of asymptomatic urethral gonococcal infection in the general population has been estimated at 1 to 3 percent [Hook and Handsfield, 1999]. Because of this high prevalence and the associated sequelae of PID, the Centers for Disease Control and Prevention have recommended guidelines for diagnosis and treatment of Chlamydial and gonococcal infection and contact tracing.

Treatment of symptomatic patients is only partially effective because of the large percentage of asymptomatic patients.

Intended Use

The GEN–PROBE® APTIMA® Adapter Kit is to be used to test male urethral specimens collected with the *GEN-PROBE® PACE® Specimen Collection Kit for Urethral or Conjunctival Specimens* or female endocervical specimens collected with the *GEN-PROBE PACE Specimen Collection Kit for Endocervical Specimens* in the APTIMA Assays.

Summary of Technological Characteristics of the APTIMA Combo 2 Assay

The APTIMA Combo 2 Assay incorporates the technologies of target capture, *in vitro* nucleic acid amplification, and hybridization of target amplicons with acridinium ester-labeled DNA probes to specifically detect and differentiate both *C. trachomatis* and *N. gonorrhoeae* nucleic acids in clinical specimens. GEN-PROBE's proprietary technologies are combined in this product to allow qualitative detection of *C. trachomatis* rRNA and *N. gonorrhoeae* rRNA.

Principles of the APTIMA Combo 2 Assay Technology

The APTIMA Combo 2 Assay utilizes Target Capture, Transcription-Mediated Amplification (TMA) and the Dual Kinetic Assay (DKA) to qualitatively detect *C. trachomatis* and *N. gonorrhoeae* (rRNA). Target Capture is a method of direct purification of target away from potential amplification reaction inhibitors. The target nucleic acid molecules are captured onto the surface of magnetic particles. Following an aspiration of the primary specimen material from the reaction tube, the particles are brought through a wash cycle prior to the addition of the amplification reagents, effectively purifying and concentrating the target nucleic acid away from the other material present in urine or endocervical /male urethral swab specimens.

TMA is an RNA transcription-dependent amplification technology, in which RNA strands serve as templates for the synthesis of DNA intermediates. These DNA intermediates are then used for the transcription of multiple copies of RNA amplicon. The RNA amplicon can then serve as templates for further synthesis of DNA intermediates, which in turn are used for further transcription of copies of RNA amplicon. The APTIMA Combo 2 Assay uses TMA to amplify specific regions of *C. trachomatis* and *N. gonorrhoeae* rRNA in clinical specimens to easily detectable levels.

DKA is identical to the Hybridization Protection Assay (HPA) used in Gen-Probe's PACE assays and Amp CT assay, except that two different chemiluminescent probes are utilized. One probe is specific for the CT amplicon and the second probe is specific to the GC amplicon. Under the detection conditions, each probe emits light at a different

relative rate resulting in a unique kinetic light-off profile. The CT probe emits light very rapidly, whereas the GC probe emits light more slowly. Examination of the kinetic profile of an APTIMA Combo 2 test by the assay software allows the presence of CT, GC or both amplicons to be determined.

Clinical Trial Results

A clinical study was conducted to establish the equivalence between APTIMA Combo 2 Assay results using the GEN-PROBE PACE Specimen Collection Kits with the APTIMA Adapter Kit and the APTIMA Combo 2 Unisex Swab Collection Kit. Assay performance was assessed by comparing the results from PACE male urethral and female endocervical swab specimens, diluted using the Transport Medium supplied in the APTIMA Adapter Kit, to the results from swab specimens collected with the APTIMA Combo 2 Unisex Swab Collection Kit. The study evaluated paired swab specimens from 154 male subjects and 232 female subjects attending STD and Family Planning clinics. A total of 772 *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoea* (GC) test results were used in the data analysis.

The percent agreement between the APTIMA Combo 2 Assay CT results using specimens collected with the PACE Swab Specimen Collection Kit and specimens collected with the APTIMA Combo 2 Swab Specimen Collection kit was 97.7% (95% C.I.: 95.6% - 98.9%). The percent agreement between the APTIMA Combo 2 Assay GC results using specimens collected with the PACE Swab Specimen Collection Kit and specimens collected with the APTIMA Combo 2 Swab Specimen Collection kit was 98.7% (95% C.I.: 97.0% - 99.6%). The results of this study demonstrate that using the APTIMA Adapter Kit with specimens collected in the PACE Specimen Collection Kits yield equivalent APTIMA Combo 2 Assay results when compared to specimens collected with the APTIMA Combo 2 Assay, Unisex Swab Specimen Collection Kits.

Conclusions from the Clinical Data

The clinical data demonstrate equivalent APTIMA Combo 2 Assay performance for PACE specimens processed with the GEN-PROBE APTIMA Adapter Kit supporting the statement of **SUBSTANTIAL EQUIVALENCE** to the FDA-cleared APTIMA Combo 2 Assay used for the detection of *C. trachomatis* and *N. gonorrhoeae* in clinical specimens.

Further, the results of this clinical study demonstrate reasonable evidence that when the GEN-PROBE APTIMA Adapter Kit is labeled as proposed, the GEN-PROBE APTIMA Adapter Kit is safe and effective for its stated intended use.

The GEN-PROBE APTIMA Adapter Kit provides diluent for PACE specimens and is specifically formulated to allow for the testing of specimens collected with the PACE collection devices in the APTIMA Combo 2 Assay. This diluent is identical to the transport media provided in both the PACE and APTIMA collection kits. The APTIMA Adapter Kit and its application allow for the inclusion of PACE specimens as acceptable testing specimens in the APTIMA Combo 2 Assay. This broadens the application of the APTIMA Combo 2 Assay as a diagnostic tool to provide information that measurably contributes to a diagnosis of *C. trachomatis* and *N. gonorrhoeae* infection. Application of the APTIMA Adapter kit provides substantially equivalent performance of the FDA-cleared APTIMA Combo 2 Assay for the detection of *C. trachomatis* and *N. gonorrhoeae* indicative of it's safety and effectiveness.

Contraindications and Cautions

There are no contraindications or cautions.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
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SEP 17 2002

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Re: k022874
Trade/Device Name: Gen-Probe® APTIMA® Adapter Kit
Regulation Number: 21 CFR 866.2900
Regulation Name: Microbiological Specimen Collection and Transport Device
Regulatory Class: Class I
Product Code: JTW
Dated: July 25, 2002
Received: July 26, 2002

Dear Dr. Maderazo:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

INDICATIONS FOR USE STATEMENT

510(k) Number (if known): _____

Device Name: GEN-PROBE® APTIMA® Adapter Kit

Indications for Use:

The GEN-PROBE® APTIMA® Adapter Kit is to be used to test male urethral specimens collected with the *GEN-PROBE® PACE® Specimen Collection Kit for Urethral or Conjunctival Specimens* or female endocervical specimens collected with the *GEN-PROBE PACE Specimen Collection Kit for Endocervical Specimens* in the APTIMA Assays.

Woody Dubois for FMP

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K050874

Prescription Use ✓